

SEP 25 2006

Atty Dkt. No.: 10031551-1  
USSN: 10/813,467REMARKS

In view of the following remarks, the Examiner is requested to allow claims 28-59, the only claims pending and under examination in this application.

Claim 28 has been amended to recite that both the monomer and polymer are attached to the substrate and that both are blocked with a blocking group. These changes are editorial in nature. Support is present in the original claims and throughout the specification. Similarly, Claim 56 has been amended to recite that the monomers are blocked with a blocking group. Claim 35 has been amended to correct a typographical error. Support is present in original Claim 2. Claim 36 has been amended to recite that the density difference is expressed as the Atwood number (A). Support is present at page 34, first complete paragraph, of Applicants' specification.

No new matter has been added.

***Claim Rejections – 35 U.S.C. § 112, second paragraph***

Claims 28-55 have been rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is respectfully traversed.

With respect to Claims 28-55, the Examiner asserted that it is unclear whether *attached* and *blocked* modify only nucleoside monomer or polymer as well. Present Claim 28 recites that *attached* and *blocked* modify both nucleoside monomer and polymer. The Examiner asserted further that the phrase *the substrate surface* in line 6 of Claim 28 lacks antecedent basis in the word *substrate* in line 1 of the claim. Applicants submit that antecedent basis is in fact present in the recitation of *substrate* because a substrate by its very nature has a surface.

Withdrawal of this aspect of the rejection is respectfully requested.

With respect to Claims 28-59, the Examiner asserted that the phrase *the blocking group* lacks antecedent basis in the phrase *blocked nucleoside monomer*.

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Present Claims 28 and 56 recite that the blocked entities are blocked with a blocking group.

Withdrawal of this aspect of the rejection is respectfully requested.

With respect to Claim 35, the Examiner asserted that the phrase *the blocking fluid* lacks antecedent basis in Claim 28. Applicants have corrected a typographical error so that present Claim 35 recites *deblocking fluid*.

Withdrawal of this aspect of the rejection is respectfully requested.

With respect to Claims 36 and 54, the Examiner appears to imply that the phrase *at least about* is *per se* indefinite where the metes and bounds of the term are not defined in the specification or claim. Applicants note that, contrary to the Examiner's assertion, this phrase does not appear in Claim 54, which recites *less than about*. Clarification is respectfully requested, because it is unclear if the Examiner considers *less than about* to be indefinite as well.

In *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200 (CAFC 1991) the court held that the phrase *at least about* was indefinite primarily because of the range of error in bioassays, not because of indefiniteness of the phrase *per se* or because of absence of a definition of the phrase in the specification.

The word *about* itself has been held definite. See, for example, *Ex parte Eastwood*, 163 USPQ 316 (BPAI 1968) and *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540 (CAFC 1983). The *Eastwood* Board considered the word *about* "clear but flexible" and "similar in meaning to terms such as 'approximately' or 'nearly'." *Eastwood* at 317.

Therefore, there is no reason why the phrase *at least about* is indefinite in the context of present Claim 36 wherein a parameter (density) that can be measured accurately is involved, unlike the bioassays in *Amgen*. The phrase *about 0.01* provides for tolerances (i.e. a narrow range) above and below 0.01, and the phrase *at least* means that those tolerances provide the minimum values. As such, there is nothing indefinite in the juxtaposition of those two phrases to form the phrase *at least about*. When the phrases *at least* and *about* are read together the meaning of *at least about* is clear. The Examiner has found indefiniteness by reading and defining

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*at least and about separately*, which is not a reasonable interpretation of the claim language.

Similarly, the phrase *less than about* in Claim 54 is not indefinite. A parameter (vapor pressure) that can be measured accurately is again involved, unlike the bioassays in *Amgen*. The phrase *about 13 Kpa* provides for tolerances (i.e. a narrow range) above and below 13 Kpa, and the phrase *less than* means less than those tolerances.

Withdrawal of this aspect of the rejection is respectfully requested.

With respect to Claim 36, the Examiner asserted that the density difference lacks units. Present Claim 36 recites that the density difference is expressed as the Atwood number.

Withdrawal of this aspect of the rejection is respectfully requested.

#### ***Claim Rejections – 35 U.S.C. § 102***

Claims 28-34, 39-43, 46-48, 50-51, and 54-59 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Gao et al. (U.S. Patent No. 6,426,184) ("Gao"). This rejection is respectfully traversed.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Moreover, an anticipation rejection that is based on inherency must be supported by factual and technical grounds establishing that the inherent feature must flow as a necessary conclusion, not simply a possible conclusion, from the teaching of the cited art. *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Int. 1990); *In re Oelrich*, 666 F.2d 578, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981).

Claims 28 and 56 recite in pertinent part *displacing the deblocking fluid ... with a purging fluid*. The Examiner asserted that Gao teaches "displacing the blocking fluid from the substrate surface comprising the attached unblocked nucleoside monomer or polymer with a purging fluid..." The Examiner directed attention to Example II and to Table 2 of Gao.

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In fact, Gao does not use the words *displacing* or *purgung fluid*. Gao discloses that methylene chloride and acetonitrile are used as *washing* solvents. As defined in Applicants' specification at page 32, last paragraph, displacing with a purging fluid is a much more complex procedure than mere washing. Displacement of the deblocking fluid in the context of the present invention involves flowing a different density purging fluid across the surface in a manner that produces a defined interface or front between the purging fluid and the deblocking fluid, which defined interface is maintained as it moves across the substrate surface and the deblocking fluid is concomitantly displaced therefrom.

The washing process of Gao is completely different from the purging process as claimed by Applicants. Applicants' claimed invention is directed, *inter alia*, to removing a deblocking fluid from a substrate. As set forth above, the deblocking fluid is removed from the substrate by being displaced or pushed with a purging fluid while maintaining a defined interface between the two fluids. The purging fluid is then removed from the surface by using any convenient fluid removal protocol. The result is that the deblocking fluid is removed (e.g., via displacement) and the attached nucleoside monomers remain intact.

In a washing process there is no defined interface between a wash fluid and whatever is being washed away by the wash fluid. Typically, the purpose of washing is the complete removal of a solid or liquid. Therefore, washing is a far less controlled process than is displacement, and there is mixing of the wash fluid and any fluid being washed away.

It is well established that during examination, the pending claims must be given their broadest reasonable interpretation consistent with the specification. MPEP § 2173.05(a). Applicants submit that to consider *displacing the deblocking fluid ... with a purging fluid* as reading on *washing* would be inconsistent with Applicants' specification.

Finally, if the Examiner considers that *displacing the deblocking fluid ... with a purging fluid* is inherently accomplished by a washing step, factual and technical grounds must be presented establishing that the inherent feature must flow as a necessary conclusion, not simply a possible conclusion, from the Gao's teaching of washing.

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Accordingly, each and every element of Applicants' claims is not described expressly or inherently in Gao. As such, there is no anticipation.

Withdrawal of this rejection is respectfully requested.

Claims 28 and 35-38 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Gao et al. as defined by the Merck Index (12<sup>th</sup> edition, Whitehouse Station NJ, pp. 11, 802, 1035, and 1574 (1996)). This rejection is respectfully traversed.

The Merck Index was cited only for its disclosure of the densities of various organic liquids disclosed in Gao. As such, the Merck index does not remedy the deficiency of Gao, detailed in the above arguments with respect to the § 102(b) rejection over Gao alone. Specifically, the Merck Index does not establish that *displacing the deblocking fluid ... with a purging fluid is the same as washing.*

Accordingly, each and every element of Applicants' claims is not described expressly or inherently in Gao, as defined by the Merck Index. As such, there is no anticipation.

Withdrawal of this rejection is respectfully requested.

#### ***Claim Rejections – 35 U.S.C. § 103***

Claims 28 and 44 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Gao et al. In view of Nagatomo et al. (U.S. Patent No. 4,282,825) ("Nagatomo"). This rejection is respectfully traversed.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation either in the cited references themselves or in the knowledge generally available to an art worker, to modify the reference or to combine reference teachings so as to arrive at the claimed method. Second, the art must provide a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations (MPEP § 2143). The teaching or suggestion to arrive at the claimed method and the reasonable expectation of success must both be found in the prior art, not in Applicant's

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disclosure (MPEP § 2143 citing with favor, *In re Vaeck*, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991)).

The Examiner acknowledged that Gao does not teach a stratified fluid interface, as in present Claim 44. Nagatomo was cited allegedly for a teaching of using a stratified fluid interface, but the Examiner appears to consider a stream (disclosed in the Abstract of Nagatomo) to be a stratified fluid interface.

Even if a stream were a stratified fluid interface, Nagatomo discloses surface treatments such as washing or etching. As such, Nagatomo does not remedy the deficiency of Gao, detailed in the above arguments with respect to the § 102(b) rejection over Gao alone. Specifically, Nagatomo does not establish that *displacing the deblocking fluid ... with a purging fluid* is the same as washing.

Accordingly, for at least the reason that the combination of cited documents does not teach or suggest all of the elements of Applicants' claims, there is no *prima facie* obviousness.

Withdrawal of this rejection is respectfully requested.

Claim 45 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Gao et al. and Nagatomo et al. as applied to Claim 44 above, and further in view of Nonomura et al. (U.S. Patent No. 6,139,708) ("Nonomura"). This rejection is respectfully traversed.

The Examiner acknowledged that neither Gao nor Nagatomo teaches flow rates from about 1 to about 20 cm/s. Nonomura was cited only for such a teaching.

As such, Nonomura does not remedy the deficiency of Gao, detailed in the above arguments with respect to the § 102(b) rejection over Gao alone. Specifically, Nonomura does not establish that *displacing the deblocking fluid ... with a purging fluid* is the same as washing.

Accordingly, for at least the reason that the combination of cited documents does not teach or suggest all of the elements of Applicants' claims, there is no *prima facie* obviousness.

Withdrawal of this rejection is respectfully requested.

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Claims 28, 33, 51 and 52 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Gao et al. in view of Fodor et al. (US Publication 2002/0137096) ("Fodor").

The Examiner acknowledged that Gao does not teach vertical flow cells, as in present Claim 52. Fodor was cited only for such a teaching.

As such, Fodor does not remedy the deficiency of Gao, detailed in the above arguments with respect to the § 102(b) rejection over Gao alone. Specifically, Fodor does not establish that *displacing the deblocking fluid ... with a purging fluid* is the same as washing.

Accordingly, for at least the reason that the combination of cited documents does not teach or suggest all of the elements of Applicants' claims, there is no *prima facie* obviousness.

Withdrawal of this rejection is respectfully requested.

Claim 53 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Gao et al. and Nagatomo et al. as applied to claim 44 above, and further in view of Farr (U.S. Patent No. 3,969,250).

The Examiner acknowledged that neither Gao nor Nagatomo teaches a pressure gradient, as in present Claim 53. Farr was cited only for such a teaching.

As such, Farr does not remedy the deficiency of Gao, detailed in the above arguments with respect to the § 102(b) rejection over Gao alone. Specifically, Farr does not establish that *displacing the deblocking fluid ... with a purging fluid* is the same as washing.

Accordingly, for at least the reason that the combination of cited documents does not teach or suggest all of the elements of Applicants' claims, there is no *prima facie* obviousness.

Withdrawal of this rejection is respectfully requested.

Claims 28-29 and 49 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Gao et al. in view of Gamble et al. (U.S. Patent No. 5,874,554) ("Gamble").

The Examiner acknowledged that Gao does not teach pulse jetting of monomers, as in present Claim 49. Gamble was cited only for such a teaching.

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As such, Gamble does not remedy the deficiency of Gao, detailed in the above arguments with respect to the § 102(b) rejection over Gao alone. Specifically, Gamble does not establish that *displacing the deblocking fluid ... with a purging fluid* is the same as washing.

Accordingly, for at least the reason that the combination of cited documents does not teach or suggest all of the elements of Applicants' claims, there is no *prima facie* obviousness.

Withdrawal of this rejection is respectfully requested.

#### **Statutory Double Patenting**

Claims 28-59 were provisionally rejected under 35 U.S.C. § 101 as allegedly claiming the same invention as that of Claims 1-3 and 7-36 of copending U.S. Application No. 11/234,701. This rejection is respectfully traversed.

Applicants respectfully directs the attention of the Examiner to MPEP § 804 IIA, which sets forth a test for double patenting under 35 U.S.C. § 101. In short, if a claim in an application could be literally infringed without literally infringing a claim in the corresponding patent, there can be no double patenting under 35 U.S.C. § 101. The test poses the question: "Is there an embodiment of the invention that falls within the scope of one claim, but not the other?" If there is such an embodiment, the subject matter is not identical, and there is no statutory double patenting.

This test will now be applied to the present situation. Claim 1 of the copending application recites a method of synthesizing a nucleic acid molecule, whereas Claim 1 of the present application recites a method of synthesizing an oligonucleotide.

Claim 1 of the copending application would be literally infringed by a synthesis of DNA on a substrate using the claimed method steps. However, Applicants define (page 5 of specification) an oligonucleotide as a single stranded multimer from about 10 to 100 nucleotides and up to 200 nucleotides in length. As such, Applicants' claims do not include DNA synthesis. Therefore, there is at least one embodiment that falls within the scope of one claim, but not the other. Accordingly, for at least this reason, there is no statutory double patenting.

Withdrawal of this rejection is respectfully requested.

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***Nonstatutory Double Patenting***

Claims 28, 30, 32-34, 39-43, 48-49, 51, 54, 55 and 56-59 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1, 3-8, and 10-18 of copending Application No. 11/082,006 in view of Wilding et al. (U.S. Patent No. 5,498,392) ("Wilding"). This rejection is respectfully traversed.

The Examiner appears to be asserting that the present rejected claims and the cited claims of the copending application are identical but for a recitation of multiple chambers. Wilding was cited only for such a teaching.

However, the claims of the copending application recite a washing step and not *displacing the deblocking fluid ... with a purging fluid*, as in the present claims. As was pointed out above in the § 102(b) rejection over Gao, the Examiner has not established that washing is the same as displacing the deblocking fluid ... with a purging fluid. Wilding does nothing to remedy this deficiency.

Accordingly, for at least the reason that the combination of cited documents does not teach or suggest all of the elements of Applicants' claims, there is no *prima facie* obviousness, and therefore no obviousness-type double patenting.

Withdrawal of this rejection is respectfully requested.

Claims 56-59 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-4 and 12-14 of copending Application No. 10/813,337. This rejection is respectfully traversed.

The Examiner appears to be asserting that the present rejected claims and the cited claims of the copending application are identical but for a recitation of two liquids in the present claims. However, Claim 1 of the copending application does not recite *displacing the deblocking fluid ... with a purging fluid*, as in the present claims. Some of the dependent claims 2-4 and 12-14 of the copending application recite sequential contacting with a plurality of liquids and/or washing.

As was pointed out above in the § 102(b) rejection over Gao, the Examiner has not established that washing (or sequential contacting) is the same as displacing

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the deblocking fluid ... with a purging fluid. Nor has the Examiner established that displacing the deblocking fluid ... with a purging fluid would have been obvious over washing.

Accordingly, for at least the reason that the cited application does not teach or suggest all of the elements of Applicants' claims, there is no *prima facie* obviousness, and therefore no obviousness-type double patenting.

Withdrawal of this rejection is respectfully requested.

Claims 28, 30, 32-33, 35-36, and 38-48 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-4 and 7-16 of copending Application No. 10/813,331.

The Examiner appears to be asserting that the present rejected claims and the cited claims of the copending application are identical but for a recitation of two liquids in the present claims. However, Claim 1 of the copending application does not recite *displacing the deblocking fluid ... with a purging fluid*, as in the present claims. Rather, Claim 1 of the copending application recites a wash fluid.

As was pointed out above in the § 102(b) rejection over Gao, the Examiner has not established that washing is the same as displacing the deblocking fluid ... with a purging fluid. Nor has the Examiner established that displacing the deblocking fluid ... with a purging fluid would have been obvious over washing.

Accordingly, for at least the reason that the cited application does not teach or suggest all of the elements of Applicants' claims, there is no *prima facie* obviousness, and therefore no obviousness-type double patenting.

Withdrawal of this rejection is respectfully requested.

Claims 28-59 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1 and 4-5 of copending Application No. 10/449,838. This rejection is respectfully traversed.

The Examiner asserted that both sets of claims are drawn to contacting a ligand array with a feature modification reagent. However, the cited copending claims are silent with respect to *displacing the deblocking fluid ... with a purging fluid*.

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as in the present claims. In fact, the cited copending claims recite only contacting an array surface with a high surface tension deposition fluid. There is no recitation of displacing with a purging fluid, nor has the Examiner established that displacing with a purging fluid would have been obvious over only contacting an array surface with a high surface tension deposition fluid.

Accordingly, for at least the reason that the cited application does not teach or suggest all of the elements of Applicants' claims, there is no *prima facie* obviousness, and therefore no obviousness-type double patenting.

Withdrawal of this rejection is respectfully requested.

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**CONCLUSION****SEP 25 2006**

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Timothy Joyce at (408) 553-2510.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1078, order number 10031551-1.

Respectfully submitted,

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